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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): SMB-004

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on November 21, 2008

Signature: [signature]

Typed or printed name: Kim Wong

Application Number	Filed
10/601,378	June 23, 2003

First Named Inventor: David Farrow

Art Unit	Examiner
1645	Karlheinz R. Skowronek

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 37,040
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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November 21, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/601,378	Confirmation No.: 7906
Applicant	:	David FARROW	
Filed	:	June 23, 2003	
TC/A.U.	:	1645	
Examiner	:	Karlheinz R. Skowronek	

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REQUEST FOR PRE-APPEAL BRIEF CONFERENCE

Sir:

The applicant respectfully requests pre-appeal brief review of the Examiner's final action mailed May 21, 2008. A Notice of Appeal is being filed herewith.

Claims 1-5, 7, 8 and 22-29 are pending, of which claims 1, 22 and 26 are independent.

Claims 1-5, 7, 8 and 22-29 remain rejected under 35 USC 103 as obvious having regard to Tullis et al., *American Clinical Laboratory* (2001) Oct/Nov, 22-23 (hereinafter "Tullis"), in view of US 6,391,657 (hereinafter "Bernhardt"), in view of US 2002/0042125 (hereinafter "Petersen"), in view of newly cited WO 01/85341 (hereinafter "Piesold"). Claims 1-5, 7, 8 and 22-29 also remain rejected under 35 USC 103 as obvious having regard to US 2004/0072278 (hereinafter "Chou"), in view of Bernhardt, in view of newly cited Piesold.

In order to maintain a rejection under 35 USC 103, the Examiner must establish 1) presence of all the claim limitations in the prior art; 2) a motivation to modify or combine the elements in the prior art to arrive at the claimed invention; and 3) a likelihood of success.

In the previous office action dated August 15, 2007, the Examiner rejected the claims *inter alia* as obvious having regard to the combination of (i) Tullis, Bernhardt and Petersen, and as obvious having regard to the combination of (ii) Chou and Bernhardt. In the final office action dated May 21, 2008, the Examiner withdrew all previous rejections in light of amendments and arguments made in Applicant's response filed February 15, 2008. Thus, the Examiner has taken the position that the current claims are <u>not</u> obvious in view of reference combinations (i) and (ii).

Accordingly, the Examiner's current position is based on the inclusion of the Piesold reference into each of reference combinations (i) and (ii).

Review of reference combinations (i) and (ii) in view of Piesold, however, reveals that neither combination discloses, describes or suggests detection of a reagent-analyte particle complex within a chamber in which the reagent-analyte complex is formed, as claimed in currently pending claim 1. The Examiner has thus failed to establish a prima facie case of obviousness.

Specifically, claim 1 as currently pending states:

> Claim 1: (previously presented) A method for detecting the presence of an analyte particle in a fluid, said method comprising, sequentially:
>
> filtering a sample of said fluid from a first chamber to a second chamber through a filter sized to pass said analyte particle and particles smaller than said analyte particle, retaining in said first chamber particles in said sample larger than said analyte particle thereby forming in said second chamber a filtered sample;
>
> adding to said filtered sample in said second chamber a reagent that specifically interacts with said analyte particle to form a reagent-analyte particle complex that is larger than said analyte particle;
>
> filtering said filtered sample from said second chamber through a filter sized to pass particles that are smaller than said reagent-analyte particle complex thereby forming in said second chamber a further filtered sample;
>
> testing said further filtered sample in said second chamber for the presence of residual particles, wherein the presence of said residual particles identifies the presence of said reagent-analyte particle complex in said second chamber, and wherein the presence of said-analyte particle complex is indicative of the presence of said analyte particle in said fluid and wherein the absence of said reagent-analyte particle complex in said second chamber is indicative of the absence of said analyte particle in said fluid.

Pending claim 1 is thus directed to a method of detection of an analyte particle in a sample using a first filtration step to remove particles larger than the analyte, specific binding of the analyte by a reagent molecule to form a reagent-analyte complex, thus increasing the apparent size of the analyte particle, followed by a second filtering step to remove particles smaller than the reagent-analyte complex. Pending claim1 specifies that the filtering occurs by passing the sample from a first chamber through a filter to a second chamber, forming a filtered sample containing particles that are the size of the analyte or smaller in the second chamber while particles larger than the analyte are removed from the filtered sample. The claim specifies that the reagent added to the second chamber is able to specifically form a reagent-analyte particle

complex, and the filtered sample is then filtered a second time to remove particles smaller than the reagent-analyte particle complex, thus forming a further filtered sample within the second chamber. The further filtered sample is then tested within the second chamber for the presence of any residue, the residue indicating that the reagent-analyte particle complex was formed, the presence of which is a positive indicator that the analyte is present in the sample fluid.

Thus, in pending claim 1, the presence of residual reagent-analyte particle complex formed during the method is used to indicate that the analyte particle is present in the original fluid. The presently claimed method tests directly for the physical presence of the reagent-analyte particle complex within a chamber in which the complex is formed, the result of which direct test indirectly indicates the presence of the analyte particle in the original fluid.

Reference Combination (i) Tullis, Bernhardt, Petersen and Piesold:

Tullis does not disclose, describe or suggest addition of a reagent molecule to an analyte particle that has been filtered to remove larger particles to form a reagent-analyte particle complex followed by a second filtering step to retain the complex within a chamber based on size and then subsequent detection of the reagent-analyte particle complex within the chamber. Rather, Tullis describes a hollow fiber device used to filter HIV particles away from larger blood cells and then capture the HIV particles with immobilized antibodies. There is no subsequent filtration step and there is no detection of the any antibody-virus complex (reagent-analyte particle complex) within the area of the device. Thus, Tullis does not disclose, describe or suggest the second filtering step and detection of the reagent-particle complex within the chamber in which it is formed, as required in pending claim 1.

Bernhardt does not compensate for the deficiencies of Tullis, as this reference does not disclose, describe or suggest detection of a reagent-analyte particle complex within the chamber in which the reagent-analyte particle complex is formed, as is required by pending claim 1. Rather, Bernhardt relates to a method for removing viral particles from an aqueous protein solution, and is mostly concerned with providing a resultant decontaminated protein solution free from virus. Bernhardt (columns 3 and 4) describes testing the filtrate after filtration, which would contain particles smaller than any reagent-analyte particle complex, but would not contain any reagent-analyte particle complex itself.

Piesold does not disclose filtering out particles larger than an analyte particle, formation of a reagent-analyte complex within a chamber or detection of residue of the reagent-analyte

particle within the chamber in which the complex is formed. Rather, Piesold merely describes a conventional flow filter device and method that uses a standard single filtration step to trap particles of a pre-determined size by allowing other species smaller than the desired particle to flow through the filter. However, there is no mention of addition of a reagent or formation of a reagent-analyte complex, filtering out particles smaller than the complex or detection of a residue of the complex within the chamber, as is required by the claims.

Petersen is merely cited for its disclosure of an injection molded plastic filter device and does not compensate for the deficiencies of Tullis, Bernhardt and Piesold.

Reference Combination (ii) Chou, Bernhardt and Piesold:

As stated above, in contrast to the present claims, Bernhardt does not describe or suggest detecting the physical presence of a formed reagent-analyte particle complex within the chamber in which the reagent-analyte particle complex is formed, the presence of which is then used to identify the presence of the analyte particle in the original fluid sample.

The Chou reference does not compensate for this defect in Bernhardt. Chou does not describe use of a reagent molecule to assist in the retention and separation of a desired analyte particle through the formation of a reagent-analyte particle complex, and then detection of the residue of a formed reagent-analyte particle complex within the chamber in which the complex is formed to act as an indirect indicator of the presence of the analyte particle in the original fluid. Chou does indicate that larger particles can be separated from smaller particles, and does indicate that once a particle has been retained in the described microfluidics device, such a particle can be analyzed by exposing the particles to desired reagents. However, Chou does not describe or suggest contacting an analyte particle with a reagent molecule to form a complex prior to further size filtration steps, nor detection of the formed complex within the chamber in which the complex is formed, as required by pending claim 1.

As stated above, Piesold does not mention addition of reagent, formation of a reagent-analyte complex, filtration of particles smaller than the complex and detection of a residue of the complex within the chamber in which the residue is formed, as required by pending claim 1.

Thus, neither of combinations (i) and (ii) discloses, describes or suggests, or provides motivation or expectation of success that would lead a skilled person to arrive at the subject matter of pending claim 1.

Appl. No. 10/601,378
Group Art Unit 1645

Applicant notes that the Examiner previously accepted that reference combinations (i) and (ii) without Piesold did not render the pending claims obvious. Applicant submits that Piesold does not compensate for the defects of previously cited reference combinations (i) and (ii).

Independent claims 22 and 26 include similar features of claim 1, but are narrower in scope than claim 1. The remaining pending claims are dependent on claim 1, 22 or 26.

Applicant appreciates that the presently claimed methods are easy to understand, and employ a novel and inventive combination of straightforward size filtration, affinity interactions and detection techniques. However, the use of straightforward techniques can provide a novel and inventive method when combined in novel and inventive ways, as is the case with the presently pending claims.

Furthermore, Applicant points out that the Examiner has needed to combine four or three references in an attempt to make a prima facie case of obviousness, and still has not been successful with either combination. Applicant submits that the need on the Examiner's part to combine such a large number of references and still failing to find all of the elements of the claims, underscores the fact that the presently claimed methods are not obvious.

In view of the foregoing, favourable reconsideration of the Final Action and claims 1-5, 7, 8 and 22-29 are respectfully requested.

Respectfully submitted,

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